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(54) **Iontophoresis system having features for reducing skin irritation**

Mit Mittel zur Verminderung der Hautreizung ausgerüstetes iontophoretisches System  
Système d'ionophorese comportant des moyens de réduction de l'irritation de la peau

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## Description

This invention relates to a system and method for iontophoretic drug delivery having features for reducing irritation to the skin of an animal and more particularly, to a system for delivery of power during iontophoretic drug delivery in a sequence for reducing skin irritation.

Iontophoresis is gaining increased acceptance as an effective method for application of ionic agents or ionic drugs through the skin of an animal. Iontophoresis can be defined as the electrically driven application of drugs or medications, in their ionic form, to the surface tissues of an animal. The application of electric current causes migration of ions into the tissue wherein such migration is proportional to the quantity of current applied through the iontophoretic system.

Skin irritation can occur during iontophoretic drug delivery. Efforts to minimize irritation have been directed to regulating the level of current, improving the electrical connection of the electrode with the skin and reducing the hydrolysis of water in the ionic medication. Irritation of the skin may be subjective wherein the iontophoretic electrode delivers so much power that it causes extreme discomfort to the patient. There are also objective indicia of irritation such as petechia, erythema and edema. Occurrence of such forms of irritation is discussed by Nancy A. Monteiro-Riviere in a paper presented in Fundamental Applied Technology, entitled "Altered Epidermal Morphology Secondary to Lidocaine Iontophoresis: In Vivo and In Vitro Studies in Porcine Skin", Vol. 15, pages 174-185 (1990).

It is known that the impedance of a patient's skin can range from over 100,000 ohms to nearly 1000 ohms, depending on the duration that the iontophoretic current is applied, the magnitude of the current which is being delivered, the location of the system on the patient's body, and other factors. In a system where the desired current level, which is determined in part by the drug administered to the patient, is one milliamp, a voltage potential of 100 volts would result if the skin impedance is 100,000 ohms. Since such a voltage would cause undesirable sensations to the user, it is highly desirable to limit the voltage across the electrodes of the iontophoretic drug delivery device to a more tolerable level.

Numerous prior art references attempt to teach iontophoretic devices which attempt to avoid irritation and/or tissue damage. US-A-4,292,968 discloses an apparatus for delivering constant current during ion therapy (iontophoresis) which will abruptly switch to delivering constant voltage when the voltage across the electrodes reaches a predetermined level. US-A-4,725,263 teaches a programmable constant current source transdermal drug delivery system wherein the current level can be adjusted or preset by trimming a circuit board in the apparatus.

However, the dual mode power source described in the US-A-4 292 968 is impractical for use with a transdermal drug delivery system. The power source disclosed in US-A-4 292 968 employs a voltage limit of 1.1 volts. While skin impedance levels in man can range as low as 1,000 ohms, more typical values during drug delivery are in the range of 5,000-10,000 ohms. This leaves a current typically in the range of 100 to 200  $\mu$ A, a level which will fail to deliver much drug.

Also, the dual mode power source first disclosed in US-A-4 292 968 provides a constant current to the electrodes of the drug delivery device, and then switches to a constant voltage if the voltage across the electrodes exceeds 1.1 volts. As described with respect to at least one embodiment of the present invention, the opposite sequence, that is, changing from a constant voltage to a constant current, takes place and is used in reducing skin irritation and burning.

US-A-4,141,359 teaches an epidermal iontophoresis device which is capable of maintaining a constant current through the epidermal tissue. To prevent excessive voltage build-up and the accompanying dangers of shock and burns, a comparative circuit monitors current flow and voltage across the electrodes and automatically triggers and SCR shut down circuit when impedance readings are outside of predetermined limits.

US-A-4 141 359 thus describes an iontophoresis power source which is a constant current source with an output voltage capable of reaching 60 volts. There is no means to prevent the voltage from reaching this level which can cause adverse sensations to the patient. Described in this patent is a safety mechanism which is activated if the patch is removed while power is being delivered. This mechanism checks the impedance of the load and turns the system off if there is a large sudden change in the impedance.

As mentioned above, it is well known that undesirable sensations will arise when voltages of this level (60 volts) are applied to the skin. To avoid these sensations, the circuit described in US-A-4 141 359 provides for the user to set the level of controlled current, and in this way avoid the sensations.

US-A-4,211,222 teaches an iontophoretic burn protection method. US-A-4 211 222 teaches the use of an electrically conductive porous intervener having a thickness which is large in relation to the thickness of the skin. This intervener is interposed between a first electrode and the skin. US-A-4 211 222 also teaches that pain and tingling due to the passage of electric current can be reduced by increasing the area of the electrode delivering the drug. US-A-4,164,226 teaches iontophoretic burn-protection electrode structures wherein one electrode of an iontophoretic system has a porous material of a thickness in excess of 3 millimeters interposed between the electrode and the skin.

US-A-4,764,164 teaches an iontophoresis device which includes an electric source including a pulse generator. The device has a circuit for discharging the charges accumulated in the electrodes during each intermission period of therapeutic pulses generated by the pulse generator. US-A-4,764,164 teaches that the device can be easily applied to

the human skin, without causing undesirable irritation in the skin, and especially without causing burns and rubefaction in the skin.

Although the prior art is replete with devices for reducing skin irritation and skin damage, the prior art efforts appear to focus on the device itself. Devices running on lower voltages, devices having intermediate pads between the electrodes and the skin, devices producing pulsating current, and devices having large electrode areas to reduce current concentration all approach the problem from a device perspective. The prior art has not attempted to understand the resistivity of the skin and develop a system that can take advantage of the natural properties of the skin in order to optimize the iontophoretic delivery while minimizing irritation and skin damages.

It is the object of the present invention to provide an improved device and method for delivering a drug iontophoretically to an animal as well as an electrical control circuit included in such an iontophoretic drug delivery system.

This object is solved, according to the invention, with the features of claims 1 and 14, respectively.

It is an advantage of the present invention to provide a drug delivery device which is attachable to a patient for supplying drug to the patient by iontophoresis, and an electronic circuit which operates with the drug delivery device to control the amount of drug and the rate at which the drug is delivered.

It is a further advantage of the present invention to provide an iontophoretic drug delivery system which minimizes or eliminates undesirable irritation, burning and rubefaction of the skin of the animal to which the system is attached.

It is yet another advantage of the present invention to provide an electronic circuit which selectively provides a controlled voltage and controlled current to the electrodes of an iontophoretic drug delivery device attachable to a patient.

It is yet a further advantage of the present invention to provide an electronic circuit which selectively provides a controlled power to the electrodes of an iontophoretic drug delivery device attachable to a patient.

It is still another advantage of the present invention to provide an iontophoresis system having an electronic circuit which monitors the current and voltage provided to the electrodes of a drug delivery device attachable to the skin of a patient for selectively controlling the amount or rate of current or voltage applied to the electrodes of the drug delivery device.

It is still a further advantage of the present invention to provide an iontophoretic drug delivery system and method which overcomes the inherent drawbacks of known systems and methods.

In accordance with the present invention, the iontophoretic drug delivery system includes a device having a drug reservoir adapted to be placed in communication with the skin of an animal and an electrolyte reservoir which is adapted to be placed in communication with the skin of the animal. The device includes two electrodes. The first electrode may be mounted at least partially in the drug reservoir, and the second electrode may be mounted at least partially in the electrolyte reservoir.

According to a further preferred embodiment of the drug delivery system includes an electronic circuit coupled to the electrodes of the device having the drug reservoir and the electrolyte reservoir, which circuit selectively provides at least one of a controlled voltage and a controlled current to the electrodes. The circuit includes an adjustable voltage and current generating circuit coupled to the electrodes, a current sensor coupled to one or more of the electrodes for sensing the current provided to the electrodes, and a voltage sensor coupled to one or more of the electrodes for sensing the voltage provided to the electrodes. The current and voltage sensors respectively generate a sensed current feedback signal and a sensed voltage feedback signal, which are representative of the electrode current and voltage sensed by the sensors.

The electronic circuit further includes a comparator circuit for comparing the sensed current feedback signal with a predetermined current threshold signal. A feedback signal selector circuit which is responsive to at least an output signal from the current comparator circuit will generate a feedback signal corresponding to at least one of the sensed current feedback signal and the sensed voltage feedback signal.

The electronic circuit further includes a setpoint selector circuit which is responsive to at least the output signal from the current comparator circuit and, in response thereto, will generate a setpoint signal corresponding to at least one of a voltage limit signal and a desired delivery current signal.

A subtractor circuit will subtract the feedback signal from the setpoint signal and generate an error signal corresponding to the difference between the two. The voltage and current generating circuit is responsive to this error signal and adjusts at least one of the current and voltage provided to the electrodes of the drug delivery device.

Another embodiment of the drug delivery system includes a biphasic power source coupled to the electrodes of the device having the drug reservoir and the electrolyte reservoir, which power source provides at least one of a constant voltage and a constant current to the electrodes. The biphasic power source preferably includes a constant current source having two outputs connected to the electrodes of the drug delivery device, and a voltage limiting circuit, such as a zener diode, coupled in parallel with the outputs of the constant current source to limit the voltage across the electrodes to a predetermined voltage.

These and other features and advantages of this invention will become apparent from the following detailed description of illustrative embodiments thereof, which is to be read in connection with the accompanying drawings, in which:

Fig. 1 is a perspective view of an iontophoretic drug delivery system of the present invention;

Fig. 2 is a partial cross-sectional view of the drug delivery device of Fig. 1 taken along line 2-2;

Fig. 3 and Fig. 4 are graphs illustrating voltage, current and power which demonstrate the operation of the present invention;

Fig. 5 is a schematic/block diagram view showing a first embodiment of a circuit for providing current for the iontophoretic delivery of the present invention;

Fig. 5A is a block diagram of a second embodiment of the electronic circuit of the iontophoresis system formed in accordance with the present invention;

Fig. 5B is a schematic/block diagram of a third alternative embodiment of the electronic circuit of the iontophoresis system formed in accordance with the present invention;

Fig. 6 is a graph illustrating a profile of current with respect to time for iontophoretic delivery of the present invention;

Fig. 7 is a graph illustrating voltage with respect to time for iontophoretic delivery using the present invention; and

Fig. 8 is a block diagram illustrating a biphasic power source of the present invention for providing a constant current and a constant voltage to the electrodes of a transdermal drug delivery device.

While this invention is satisfied by embodiments in many different forms, there are shown in the drawings and will herein be described in detail preferred embodiments of the invention with the understanding that the present disclosure is to be considered exemplary of the principles of the invention.

Adverting to Figs. 1-8, an operable iontophoretic drug delivery system/device 20 includes a drug reservoir 21 adapted to be attached to the skin of an animal, a first electrode 22 in the drug reservoir, an electrolyte reservoir 23 adapted to be attached to the skin of an animal and a second electrode 25 in the electrolyte reservoir.

For the purposes of the description of the present invention, the term "proximal" or "lower" is meant to refer to the side of the device closest to the skin, whereas the term "distal" or "upper" is meant to refer to the side of the device or element which is furthest from the skin.

For the purpose of description of the present invention and the claims, the term "animal" as used herein shall include all living beings including humans. The term "irritation" as used herein shall mean subjective irritation such as pain and tingling and objective irritation such as petechia, erythema and edema.

In this embodiment, the entire housing is made of insulating material, such as plastic.

Drug reservoir 21 is capable of holding an ionic compound such as a therapeutic compound, a diagnostic compound and a drug. In many cases, the ionic compounds are ionic liquids, however, the compound may be in the form of a gel or may be contained in the reservoir along with other materials such as porous polymeric structures. For the purpose of the description of this invention, drug reservoir 21 contains a therapeutic liquid 29. This therapeutic liquid does not limit the invention but is intended to be representative of these many possibilities for an ionic compound which can be delivered iontophoretically.

Electrolyte reservoir 23 contains electrolyte solution 31. The electrolyte solution may be in the form of a liquid or a gel, or may be contained in the reservoir along with other materials such as porous polymeric material.

Lower surface 32 of the housing contains an adhesive coating 33 for attaching the housing to the skin of an animal. A removable release sheet 34 is provided to protect the adhesive before time of use and for helping to contain the therapeutic liquid and the electrolyte in the reservoirs before time of use.

The drug delivery device shown in Figs. 1 and 2 further includes conductors 35 and 37 which are respectively connected to electrodes 22 and 25 and to the electronic circuit of the iontophoresis system of the present invention. The conductors may be made of silver, silver/chloride, gold, copper, molybdenum, lead or other suitable conductive materials.

A substantial difference between the iontophoretic drug delivery device of the present invention and the prior art lies in the electronic circuitry, one form of which is shown in Fig. 5. To fully understand the major structural and functional differences between the device of the present invention and the prior art it is important to understand the properties of the skin into which ions are driven by an iontophoretic drug delivery device. The electrical impedance of the skin greatly affects the occurrence of irritation and tissue damage. The electrical impedance of epidermal tissue is highly variable, depending on such factors as location on the body, presence of calluses or dermal abrasions, ambient air con-

ditions such as temperature and humidity, state of hydration which may be caused by perspiration, and the age, sex and race of the individual. It is known that the dose of an ionic substance delivered to an individual is in general proportional to the electric current. In efforts to increase the dose of ionic substance or reduce the time over which a given dose may be administered, the electric current is often raised to a level which results in skin irritation and skin damage including burns. For example, in US-A-4,141,359 native values of skin impedance of 10,000 to 50,000 ohms are disclosed. If a modest current of 3 milliamperes is caused to flow through skin with an average value of 30,000 ohms, the required voltage by Ohms' Law would be 30,000 ohms time 0.003 amperes or 90 volts. Such a voltage is widely known to be capable of causing irreversible skin breakdown, which is believed to provide low resistance paths, and hence paths where high levels of energy are dissipated in the skin. This high level of energy is believed to cause burns.

During iontophoresis episodes, the impedance of skin through which ions are transferred is initially at a high value, and then steadily decreases. The instant invention provides a device and a method for effective iontophoretic delivery while minimizing irritation and burns by accommodating the highly variable nature of skin impedance.

The method and the device of the instant invention work as follows. An iontophoretic delivery device such as device 20 is attached to the skin of an animal. The attachment can be accomplished by removing the backing sheet and pressing the device against the skin. Next, electrical power is caused to flow between the electrodes at a constant voltage  $V_0$  as illustrated in Figs. 3 and 7.  $V_0$  is of a sufficiently low magnitude not to cause irritation to the skin. Because the initial high impedance of skin, the current is at a low value during this time as illustrated in Fig. 6. Because current is flowing, the skin impedance begins to fall allowing more current to flow. This in turn causes the skin impedance to decrease further, which permits more current to flow, and so on as illustrated in Fig. 6. At time T in Fig. 6 the current reaches the pre-selected value of  $I_0$ . When  $I_0$  is reached, the electronic circuit, supplying a controlled voltage  $V_0$  to the electrodes, as will be explained in more detail hereinafter, switches modes and becomes a constant current source (see Figs. 6 and 7). Fig. 6 illustrates the rise of current to  $I_0$  at which time current becomes constant at  $I_0$ . When  $I_0$  is reached, and the system delivers constant current  $I_0$ , the voltage begins falling. This falling off of voltage from the  $V_0$  value is due to the decreasing resistance of the skin. The instant invention functions such that the voltage is prevented from rising to a level which can cause irreversible skin breakdown which leads to burns. At the same time, the desirable constant current capability is provided once the switchover to  $I_0$  is achieved.

Accordingly, the instant invention may be used by attaching an iontophoretic drug delivery device to the skin, as described hereinabove, and to at least initially impress a constant voltage across the electrodes of the device. The current flowing through the electrodes is monitored while the constant voltage is applied. The electronic circuit senses when the monitored current reached a predetermined current, such as  $I_0$ , and switches from supplying a constant voltage to the electrodes to supplying a constant current,  $I_0$ . This current continues to flow between the electrodes, at a constant predetermined rate, until the therapy regimen is completed.

It is known that there is a relationship between the current delivered to the electrodes and the quantity of ions transferred through the skin. Accordingly, the amount of current with respect to time can be measured to determine the amount of drug transferred through the skin. When using the method of the instant invention, the user can monitor the total current (over time) flowing between the electrodes and terminate power to the electrodes when the total amount of current, corresponding to the delivery of the desired amount of ionic compound into the skin, has been achieved.

It is known that high values of voltage and current will cause irritation and skin burning. Therefore, the present invention also provides a method and a device for limiting the amount of power that can be transmitted through the electrode system. As illustrated in Fig. 3, in some instances, the desirable power limit shown by the current designated  $P_0$  is beyond the desirable values for  $V_0$  and  $I_0$ . However, in other circumstances if the iontophoretic delivery was carried out at  $V_0$  until the value of  $I_0$  was reached, irritation may be caused to the skin. Accordingly, as best illustrated in Fig. 4, the present method and device incorporates safeguards so that in carrying out the transition from constant voltage to constant current, a predetermined constant power  $P_1$  is not exceeded. In carrying out the method of the instant invention, the power supplied to the electrodes is monitored throughout the delivery of current at constant voltage  $V_0$ . If the power reaches a predetermined value, the voltage is lowered along the constant power curve  $P_1$  until the desired  $I_0$  value is reached, as illustrated in Fig. 4. As will be explained in greater detail, the instant invention includes circuitry to implement the transition between constant voltage and constant current along a constant power curve.

One form of the electronic circuit for providing a controlled voltage, current or power to the electrodes of the drug delivery device 20 is shown in Fig. 5. The electronic circuit includes a set point selector circuit 50. Set point selector circuit 50 functions as an electronic, single pole, triple throw switch. The set point selector circuit includes: three inputs which are the poles of the switch; an output, which is effectively connected to the wiper of the switch; and a control input, which effectively controls the position of the wiper and its connection to one of the poles of the circuit.

Three predetermined voltage level signals are provided on the inputs of the set point selector circuit 50. A first voltage level is provided on a first input and represents a first power limit signal which is the maximum amount of power which is desired to be supplied to the electrodes of the drug delivery device 20. A second predetermined voltage level is provided to a second input of the set point selector circuit 50 and represents a first voltage limit signal, that is, the maximum voltage which is to be supplied to the electrodes of device 20. A third predetermined voltage level is provided

to the third input of the set point selector circuit 50 and represents the desired delivery current, that is, the constant current which is desired to flow between the electrodes of device 20. One of these predetermined voltage level signals on the three inputs of the set point selector circuit 50 will be passed through the selector circuit to the output in response to a control signal provided to the control input of the set point selector circuit. Accordingly, the set point selector circuit 50 provides a set point signal on its output which is, effectively, a predetermined voltage level.

The electronic circuit further includes a feedback selector circuit 52. Feedback selector circuit 52 is similar in many respects to the set point selector circuit 50. It functions electronically as a single pole, triple throw switch, having three separate inputs which are the poles of the switch, a single output (connected effectively to the wiper of the switch), and a control input which effectively controls the position of the wiper and the connection between the output of the feedback selector circuit and one of its three inputs.

Three voltage levels are provided on the inputs of feedback selector circuit 52. The first voltage level is provided to the first input and is a sensed current feedback signal. The second voltage level is provided to the second input of the feedback selector circuit 52 and is a sensed voltage feedback signal. The third voltage level is provided to the third input and is a sensed power feedback signal. As will be explained in greater detail, each of these signals results from monitoring and measuring the current and voltage provided to the drug delivery device 20 by the electronic circuit. The output of the feedback selector circuit 52 provides a feedback signal which, as will be explained, is compared to the set point signal in a summer or subtractor circuit 53.

The voltage and current supplied to the drug delivery device 20 are monitored by differential amplifiers 54 and 56. The first differential amplifier 54 has each of its two inputs coupled to one of the electrodes of the transdermal drug delivery device 20. The output of the amplifier 54 provides a sensed voltage feedback signal, as described previously, which varies proportionally to the voltage supplied across the electrodes of device 20.

The second differential amplifier 56 has its two inputs connected across a current sense resistor 58 which is connected in series with one of the electrodes of device 20. The current flowing through the electrodes will also flow through current sense resistor 58, which is a fixed resistor of relatively low value, and will cause a voltage drop across the resistor, which is sensed by second differential amplifier 56. The output of the second differential amplifier 56 provides a sensed current feedback signal, as described previously. The sensed voltage and current feedback signals are provided to the respective inputs of feedback selector circuit 52.

The electronic circuit of the iontophoresis system further includes a multiplication circuit 60. Multiplication circuit 60 includes two inputs on which are provided the sensed current feedback signal and the sensed voltage feedback signal. The multiplication circuit 60 multiplies the two feedback signals and provides a sensed power feedback signal on its output. The sensed power feedback signal is provided to one of the inputs of the feedback selector circuit 52, as described previously.

Set point selector circuit 50 and feedback selector circuit 52 are controlled by a set point and feedback control logic circuit 62. Set point and feedback control logic circuit 62 generates a control signal which is provided to the control inputs of each of the set point selector circuit 50 and feedback selector circuit 52. The set point and feedback control logic circuit 62 may, in one form, be a read only memory (ROM), having preferably three inputs. On one input is provided a current state signal, and on another input is provided a power state signal, and on a third input is provided a voltage state signal. Each of the current state signal, and voltage state signal and power state signal is preferably a logic signal, and the control signal generated by the set point and feedback control logic circuit 62 is also preferably a logic signal.

The electronic circuit of the iontophoresis system further includes a first and second comparator 64 and 66, and in a preferred form of the invention, a third comparator 67. First comparator 64 generates the current state signal on its output, and second comparator 66 generates the power state signal on its output. Third comparator 67 generates the voltage state signal on its output. First comparator 64 is provided with a current limit signal, which may be in the form of a selectable DC voltage, on one of its inputs. The current limit signal may be equal to the desired delivery current signal provided to the set point selector circuit 50. The other input of the first comparator 64 is provided with the sensed current feedback signal.

Similarly, second comparator 66 is provided with a second power limit signal, which may be in the form of a preselected voltage level, on one of its inputs. The second power limit signal may be equal to the first power limit signal provided to the set point selector circuit 50. The other input of the second comparator 66 is provided with the sensed power feedback signal generated by multiplier circuit 60.

The third comparator 67 is provided with a second voltage limit signal, which may be in the form of a preselected voltage level, on one of its outputs. The second voltage limit signal may be equal to the first voltage limit signal provided to the set point selector circuit 50. The other input of the third comparator 67 is provided with the sensed voltage feedback signal.

The current state signal will be at one logic level when the current limit signal is greater than the sensed current feedback signal provided to the first comparator 64, and will be in a second logic state when the current limit signal is less than or equal to the sensed current feedback signal. Similarly, the power state signal will be in one logic state when the second power limit signal is greater than the sensed power feedback signal provided to the second comparator 66,

and will be in a different state when the power limit signal is less than or equal to the sensed power feedback signal. The voltage state signal will be in one logic state when the second voltage limit signal is greater than the sensed voltage feedback signal provided to the third comparator 67, and will be in a different state when the voltage limit signal is less than or equal to the sensed voltage feedback signal.

Set point and feedback control logic circuit 62 is preprogrammed to provide different control signals in response to the different conditions of the current state signal and the second power state signal and, if the third comparator 67 is included in the second voltage limit signal. If the sensed current feedback signal and the sensed power feedback signal are respectively below the current limit signal and the second power limit signal provided to the first and second comparators 64 and 66, set point and feedback control logic circuit 62 will generate a control signal which will cause set point selector circuit 50 and feedback selector circuit 52 to provide respectively a set point signal and feedback signal which are equal or correspond to the first voltage limit signal (provided to the set point selector circuit 50) and the sensed voltage feedback signal (provided to the feedback selector circuit 52). If the sensed current feedback signal is below the current limit signal provided to first comparator 64, and the sensed power feedback signal is greater than or equal to the second power limit signal provided to second comparator 66, set point and feedback control logic circuit 62 will provide a control signal which will cause set point selector circuit 50 and feedback selector circuit 52 to provide respectively a set point signal and a feedback signal which are equal or correspond to the first power limit signal provided to the set point selector circuit 50 and the sensed power feedback signal provided to feedback selector circuit 52.

If the sensed current feedback signal is greater than or equal to the current limit signal provided to first comparator 64, and the sensed power feedback signal is less than the second power limit signal provided to the second comparator 66, the set point and feedback control logic circuit 62 will provide a control signal to the set point selector circuit 50 and the feedback selector circuit 52 such that the set point selector circuit and the feedback selector circuit will respectively generate a set point signal and feedback signal which are equal or correspond to the desired delivery current signal provided to the set point selector circuit 50 and the sensed current feedback signal provided to feedback selector circuit 52. If the sensed current feedback signal is greater than or equal to the current limit signal provided to the first comparator 64, and the sensed power feedback signal is greater than or equal to the power limit signal provided to second comparator 66, set point and feedback control logic circuit 62 will generate a control signal which will cause the set point selector circuit and the feedback selector circuit to generate respectively a set point signal and a feedback signal which are equal or correspond to the first power limit signal provided to set point selector circuit 50 and the sensed power feedback signal provided to feedback selector circuit 52.

It is possible that the impedance of the patient's skin may increase while the transdermal delivery system is operating in the constant current mode. This will cause the voltage delivered to the patient to increase, possibly causing discomfort, or even injury if a power limit is not used. Under such circumstances, it may be desirable for the circuit to switch back into a controlled, constant voltage mode. The third comparator 67 may be included for such a purpose. Thus, if the sensed voltage feedback signal equals or exceeds the second voltage limit provided to the third comparator 67, the set point and feedback control logic circuit 62 will provide a control signal to the set point selector circuit 50 and the feedback selector circuit 52 such that the set point selector circuit and the feedback selector circuit will respectively generate a set point signal and feedback signal which are equal or correspond to the first voltage limit signal (provided to the set point selector circuit 50) and the sensed voltage feedback signal (provided to the feedback selector circuit 52).

Of course, it should be realized that the set point and feedback control circuit 62 will cause the delivery system to go into a controlled constant power mode if the sensed power feedback signal equals or exceeds the second power limit signal provided to the second comparator 66. This will occur whether or not the current limit signal or the second voltage limit signal is exceeded.

The following table illustrates the mode which the circuit will be in response to whether the sensed current, voltage and power feedback signals are above or below their respective threshold limits provided to comparators 64, 66 and 67.

TABLE 1

C	V	P	MODE
Below Limit	Below Limit	Below Limit	Voltage
Above or Equal to Limit	Below Limit	Below Limit	Current
Below Limit	Above or Equal to Limit	Below Limit	Voltage
Above or Equal to Limit	Above or Equal to Limit	Below Limit	Voltage

TABLE 1 (continued)

C	V	P	MODE
X	X	Above or Equal to Limit	Power
C = sensed current feedback signal V = sensed voltage feedback signal P = sensed power feedback signal X = "don't care" condition			

It should be noted that an alternative form of the invention would omit the power mode and its related structure such as comparator 66, multiplication circuit 60 and the first and second power limit signals. The circuit would include the structure described previously, including comparators 64 and 67, which would allow the circuit to switch between a controlled, constant current mode and a controlled constant voltage mode.

As mentioned previously, the set point signal and feedback signal are provided to a summer or subtractor circuit 53. Summer or subtractor circuit 53 will subtract the feedback signal from the set point signal and provide an error signal on its output, which error signal corresponds to the difference in voltage levels between the set point signal and the feedback signal.

The error signal from the summer circuit 53 is, in one form of the invention, provided to the input of a variable pulse generator 68, such as a voltage controlled oscillator (VCO). Variable pulse generator 68 provides a pulsed output signal which varies in either frequency or duty cycle proportionally to the magnitude of the error signal generated by summer circuit 53.

The electronic circuit of the iontophoresis system further includes a pulse to power converter circuit 70. Pulse to power converter circuit 70 includes an input to which is provided the output signal from variable pulse generator 68, and a pair of outputs across which is a controlled voltage which is generated by the pulse to power converter circuit from a power source 72 connected to another input of the converter circuit 70. The output voltage generated by pulse to power converter circuit 70 across its outputs will vary in accordance with the frequency or duty cycle of the pulsed output signal from the pulse generator 68 and, in turn, the voltage level of the error signal generated by summer circuit 53.

An alternative embodiment of the system circuit is shown in Fig. 5A. The pulse generator 68 and pulse to power converter circuit 70 may be replaced with a power amplifier circuit 73. The power amplifier circuit 73 includes an input which receives the error signal from summer circuit 53, and generates an output voltage which varies in response to the error signal. The output voltage is provided to the drug delivery device 20 in a manner similar to that which is described in relation to the embodiment of Fig. 5.

The portion of the electronic circuit of the iontophoresis system thus described provides a selectable, controlled constant voltage, constant current or constant power to the electrodes of the transdermal drug delivery device 20, as described previously, through feedback. When the iontophoresis system is initially applied to the patient, the current sensed by the circuit flowing through the electrodes will be at a relatively low level, that is, less than the  $I_0$  threshold, because of the relatively high resistance of the patient's tissue. Under such conditions, the electronic circuit will be in a constant voltage mode so as to provide a constant voltage to transdermal delivery device 20. The sensed voltage feedback and the voltage limit signal will, effectively, be compared in summer circuit 53, and any differences between the two will be adjusted for by pulse to power converter circuit 70 (or power amplifier circuit 73, as shown in Fig. 5A).

When the sensed current feedback signal rises to the level of the current limit signal, because of the decrease in the resistance to the patient's tissue, the electronic circuit will switch into a constant current mode. The control signal generated by set point and feedback control logic circuit 62 will cause the delivery current signal and the sensed current feedback signal to be provided to summer or subtractor circuit 53 in order to control variable pulse generator 68 driving pulse to power converter circuit 70. Any differences between the desired delivery current signal and the sensed current feedback signal will be adjusted for by pulse to power converter circuit 70 and the feedback loop of the electronic circuit.

If, either in the constant voltage mode or the constant current mode, the sensed power feedback signal equals or exceeds the second power limit signal, set point and feedback control logic circuit 62 will generate a control signal such that the electronic circuit will go into a constant power mode. The control signal will cause the first power limit signal and the sensed power feedback signal to be provided to the inputs of summer or subtractor circuit 53, and any differences between the two will be adjusted for by pulse to power converter circuit 70 (or power amplifier circuit 73) and the feedback loop of the electronic circuit.

The iontophoresis system of the present invention indirectly monitors and measures the total quantity of the drug provided transdermally to the patient, and will stop delivery when a selectable, predetermined total dosage level is reached. More specifically, the electronic circuit includes an output enable switch circuit 74 in the form of an electronic, single pole, single throw switch, which is connected between one output of the pulse to power converter circuit 70 (or amplifier 73 in the embodiment of Fig. 5A) and one of the electrodes of the drug delivery device 20. The position of the

"wiper" of output enable switch circuit 74 is controlled by a dose state signal provided to the control input of the switch. Preferably, the dose state signal is a logic signal which is generated by a fourth comparator 76 on its output, and is provided to switch circuit 74 partially along dashed line 78, which bypasses an output enable logic circuit 80 of an alternative form of the present invention, as will be described in greater detail.

5 Fourth comparator 76 includes at least two inputs. A total dosage signal, which may be in the form of a preselected voltage level, is provided on one input, and an accumulated current signal, which may also be in the form of a variable voltage level, is provided to the other input of the fourth comparator 76.

The electronic circuit further includes an accumulator circuit 82. The accumulator circuit 82 has an input on which is provided the sensed current feedback signal, an output on which is provided the accumulated current signal. Accumulator circuit 82 effectively integrates and accumulates the sensed current feedback signal over time. It may be in the form of a circuit in which the sensed current feedback signal is converted from a voltage to a current which accumulates charge on a capacitor, the resulting voltage across the capacitor increasing in proportion to the current flowing into it. The voltage across the capacitor may be used in generating the accumulated current signal.

The accumulated current signal, which is in the form of a variable voltage level, is proportional to the current flowing through the electrodes of the transdermal drug delivery device 20, which current, in turn, is representative of the total drug dose administered to the patient. If the accumulated current signal is below the total dose signal, the dose state signal generated by fourth comparator 76 will be in one state and will cause output enable switch circuit 74 to maintain the connection between pulse to power converter circuit 70 (or amplifier 73) and one of the electrodes of delivery device 20. If the accumulated current signal equals or exceeds the total dose signal, the dose state signal will be in another state which will cause the output enable switch circuit 74 to open, disconnecting the pulse to power converter circuit 70 (or amplifier 73) from drug delivery device 20. Accordingly, the electronic circuit of the iontophoresis system will automatically disconnect power to drug delivery device 20 when the proper drug dosage has been administered to the patient.

In a preferred form of the present invention, the electronic circuit may further include an over-current shut down comparator circuit. This circuit disables the output of the pulse to power converter circuit 70 (or amplifier 73) in the event that the sensed current feedback signal exceeds a predetermined level, which preferably corresponds to 1.5 times the current delivered to the electrodes of drug delivery device 20.

More specifically, the over-current shut down comparator circuit includes an output enable logic circuit 80, which may be in the form of a ROM, which is interposed between the output of the fourth comparator 76 and the control input of output enable switch circuit 74. The output enable logic circuit 80 provides an output enable signal to output enable switch circuit 74 to control the position of the switch circuit in much the same way as the dose state signal from fourth comparator 76 did in the previous embodiment.

The dose state signal from fourth comparator 76, in this embodiment, is provided to one input of output enable logic circuit 80. An excess current limit signal, which may be in the form of a logic signal, is provided to another output of output enable logic circuit 80. The excess current limit signal is generated by a fifth comparator 82 on its output.

Fifth comparator 82 includes two inputs. One input is provided with an excess current threshold signal, which may be in the form of a pre-selected voltage level which may be equal to 1.5 times the voltage level of the desired delivery current signal. The second input is provided with the sensed current feedback signal.

The output enable logic circuit 80 will control the state of output enable switch circuit 74 in response to whether a total dose has been administered to the patient or whether the instantaneous, sensed current feedback signal exceeds the excess current threshold signal. More specifically, if the accumulated current signal is less than the total dose signal, the output enable signal generated by output enable logic circuit 80 will be such as to cause output enable switch circuit 74 to maintain a connection between the pulse to power converter circuit 70 (or amplifier circuit 73) and drug delivery device 20.

Irrespective of whether the total dose has been administered to the patient, if the sensed current feedback signal equals or exceeds the excess current threshold signal, fifth comparator 82 will provide an output signal to output enable logic circuit 80 which, in turn, will cause the output enable signal to open the output enable switch circuit 74, thereby disconnecting the pulse to power converter circuit 70 (or amplifier 73) from the drug delivery device 20. If, of course, the excess current threshold signal has not been exceeded or reached by the sensed current feedback signal and the total dose signal is greater than the accumulated current signal, the output enable logic circuit 80 will cause the output enable switch circuit 74 to maintain a connection between the pulse to power converter circuit 70 (or amplifier 73) and the drug delivery device 20. Thus, the electronic circuit of the iontophoresis system will automatically disconnect power from drug delivery device 20 if either the total dose has been administered to the patient or an excess current condition has been detected.

The circuits shown in Fig. 5 and 5A and described previously provide a controlled, constant direct current or voltage to the transdermal drug delivery device 20. However, it is envisioned to be within the scope of the invention to include a circuit which provides a controlled pulsed voltage or current to delivery device 20. Such a current is shown in Fig. 5B.

The pulse version of the circuit would include a variable pulse generator 68a, or the combination of a pulse gener-

ator 68a and power amplifier circuit 73, as shown in Fig. 5A, in lieu of the pulse to power converter circuit 70. The variable pulse generator 68a provides a pulsed output signal which varies in either frequency or duty cycle, or in amplitude at a constant frequency or duty cycle, proportionally to the magnitude at a constant frequency or duty cycle, proportionally to the magnitude of the error signal generated by the summer circuit 53.

First and second pulse to DC converter circuits 86,88 are respectively interposed in the circuit between amplifiers 56 and 54 and the feedback selector circuit 52. The pulse to DC converter circuits 86,88 are essentially averaging circuits or integrators which receive the output signals from amplifiers 56,54 and provide on their output a sensed current feedback signal and sensed voltage feedback signal which correspond to the average value of the pulsed current and pulsed voltage provided to the delivery device 20 and monitored by amplifiers 56 and 54. Thus, the sensed current and voltage feedback signals are DC signals which vary in magnitude proportionally with the pulsed current and voltage provided to delivery device 20 by variable pulse generator 68a and a power amplifier circuit 73. The remainder of the pulse version of the iontophoresis system circuit has the same structure and functions in the same way as the circuits described previously and shown in Figs. 5 and 5A.

Another embodiment of the electronic circuit for providing a constant voltage and constant current to the electrodes of the drug delivery device 20 is a biphasic power source shown in Fig. 8. The biphasic power source includes a constant current source 81 having two outputs which are connected to the positive and negative electrodes 22 and 25 of the drug delivery device 20, and a voltage limiting circuit 83 connected in parallel with the outputs of the constant current source 81.

In one form of the invention, the voltage limiting circuit 83 is a zener diode 85 arranged with its anode connected to the negative electrode 25 and its cathode connected to the positive electrode 22.

The circuit operates in the following manner. When the iontophoresis system is first turned on, the skin impedance is very high. Since the power source is a constant current source, it puts out a given desired amount of current. If the zener diode 85 was not present, the voltage across the skin would be very large. With the zener diode present, the voltage rises until the zener diode starts to conduct. The zener diode 85 then passes all the current which the skin cannot conduct at that voltage, and thereby limits the voltage across the skin. As time passes, the skin impedance falls. At some point, when the skin impedance is sufficiently low, the skin can take all the current from the constant current source 81 at a voltage less than that of the zener diode 85. As far as the above circuit is concerned, the zener diode is now "out of the circuit" since the voltage is below the point where it conducts.

Thus, it can be seen that the biphasic power source of the present invention operates in two modes--a constant voltage mode and a constant current mode. Also, it should be noted that the mode change is dictated by the skin impedance of the animal. The biphasic power source supplies a constant voltage to the positive and negative electrodes 22, 25 when the skin impedance of the animal is at least equal to a predetermined level, and supplies a constant current to the electrodes when the skin impedance of the animal is less than the predetermined level.

The skin impedance at which one desires to switch modes is dependent upon a number of factors, including the effective area of the drug reservoir 21 in contact with the patient's skin, the magnitude of the constant current delivered to the drug reservoir over the effective skin contact area, and the voltage across the electrodes 22, 25 of the drug delivery device at the time of switching from the constant voltage mode to the constant current mode.

For example, if the drug reservoir skin contact area is 5 square centimeters and the current provided to the drug reservoir is 200  $\mu$ A/square cm (for a total current of 1 ma), and the voltage across the electrodes at the time of switching modes is 6 volts, then the predetermined skin impedance is 6,000 ohms.

If, on the other hand, a 1 square centimeter (contact area) "patch" is employed which is driven by a current of 100  $\mu$ A/square cm (for a total current .1 ma), and the voltage across the electrodes at the time of switching modes is 20-volts, then the predetermined skin impedance is 200K ohms for switching.

It has been found that the voltage during transdermal drug delivery treatment should be between about 3 and about 30 volts and, more preferably, between about 6 and about 20 volts to achieve effective drug delivery rates while avoiding discomfort to the patient. Accordingly, the zener diode 85 should be selected to have a breakdown voltage in those ranges. Of course, it is envisioned that other devices than zener diode 85 may be used for voltage limiting means 83. Such devices may include shunt regulators and other similarly performing devices. It is preferred if each of these devices limits the voltage on the electrodes to between about 3 and about 30 volts and, more preferably, between about 6 and about 20 volts, as mentioned previously.

## Claims

1. An operable iontophoretic drug delivery system comprising a drug reservoir (21) adapted to be attached to the skin of an animal, a first electrode (22) in said drug reservoir (21), a second electrode (25) adapted to be brought in electrical connection with said animal, circuit means for providing electrical communication between said first and second electrodes (22,25), said circuit means including means for connecting to a source of electrical power, said circuit means comprising supply means for providing controlled constant current to one of said electrodes (22),

## characterized by

an electrolyte reservoir (23) adapted to be placed in communication with the skin of said animal, said second electrode (25) being positioned within said electrolyte reservoir, said circuit means further comprising a first supply means for providing controlled constant voltage between said electrodes (22,25) when the device is activated, said circuit means including means for monitoring current through one of said electrodes (22), and switching means, in said circuit means, for switching from a first mode wherein said first supply means provides constant voltage to a second mode wherein a second supply means provides constant current, when said current monitored by said monitoring means reaches a predetermined value.

2. The operable iontophoresis drug delivery system of claim 1, wherein said drug reservoir (21) contains an ionic compound selected from the group consisting of therapeutic compounds, diagnostic compounds and drugs, and wherein said first electrode (22) includes a conductive element selected from the group consisting of silver, silver/chloride, gold, copper, molybdenum and lead.
3. The operable iontophoretic drug delivery system of claim 1 or 2, further including power limiting means, in said switching means, for causing a transition from one of constant voltage and constant current to a constant power provided to the first and second electrodes (22,25) if a predetermined power is reached.
4. The operable iontophoresis drug delivery system of one of claims 1-3, further including means for measuring the current passing through said first electrode (22) and for accumulating the total current passing through said first electrode.
5. The operable iontophoresis drug delivery system of claim 4, further including means for terminating power to said first electrode (22) when accumulated total current reaches a predetermined value.
6. The operable iontophoretic drug delivery system according to one of claims 1-5, wherein the circuit means comprises an electronic circuit, said electronic circuit comprising:

adjustable voltage and current generating means (68,70) coupled to the electrodes (22,25) of the drug delivery device (20) and providing one of a selectively adjustable current and voltage to the electrodes (22,25),

means for sensing the current (56,58) provided to the electrodes (22,25) of the drug delivery device (20), the current sensing means (56,58) generating a sensed current feedback signal which is proportional to the sensed electrode current,

means (54) for sensing voltage provided to the electrodes of the drug delivery device (20), the voltage sensing means (54) generating a sensed voltage feedback signal which is proportional to the sensed electrode voltage,

means (64) coupled to the current sensing means (56,58) for comparing the sensed current feedback signal with a predetermined current threshold signal and generating a current state signal in response to the comparison thereof,

feedback signal selector means (52), the feedback signal selector means (52) being responsive to at least the current state signal and receiving at least the sensed current feedback signal and sensed voltage feedback signal and generating a feedback signal corresponding to at least one of the sensed current feedback signal and the sensed voltage feedback signal in response to at least the current state signal,

setpoint selector means (50), the setpoint selector means (50) receiving a preselected voltage limit signal and preselected desired drug delivery current signal and being responsive to at least the current state signal, the setpoint selector means (50) generating a setpoint signal corresponding to at least one of the voltage limit signal and the desired delivery current signal in response to at least the current state signal,

means (53) for subtracting the feedback signal from the setpoint signal, the subtracting means generating an error signal corresponding to the difference between the feedback signal and the setpoint signal, and

the voltage and current generating means (68,70) being responsive to the error signal and adjusting at least one of the current and voltage provided to the electrodes (22,25) in response thereto.

7. The operable iontophoretic drug delivery system of claim 6 wherein the adjustable voltage and current generating means (68,70) includes a variable pulse generator (68) and a pulse to power converter (70) coupled to the variable pulse generator (68), the variable pulse generator (68) being responsive to the error signal and generating a pulsed output signal which varies in correspondence to the error signal, the pulse to power converter (70) being responsive to the output signal of the variable pulse generator (68) and generating an output voltage which varies in correspondence to the pulse generator (68) output signal.

8. The operable iontophoretic drug delivery system of claim 6 or 7 wherein the electronic circuit further comprises:

multiplication means (60), the multiplication means receiving the sensed current feedback signal and the sensed voltage feedback signal and effectively multiplying the sensed current feedback signal and sensed voltage feedback signal together and generating a sensed power feedback signal in response to the multiplication thereof, the sensed power feedback signal being provided to the feedback signal selector means (52), and

means (66) coupled to the multiplication means (60) for comparing the sensed power feedback signal with a predetermined first power limit signal and generating a power state signal in response to the comparison thereof,

wherein the feedback signal selector means (52) is responsive to one of the current state signal and the power state signal, the feedback signal generated by the feedback signal selector means (52) corresponding to one of the sensed current feedback signal, the sensed voltage feedback signal and the sensed power feedback signal in response to one of the current state signal and the power state signal, and

wherein a preselected second power limit signal is provided to the setpoint selector means (50), the setpoint selector means (50) being responsive to one of the current state signal and the power state signal, the setpoint signal generated by the setpoint selector means (50) corresponding to one of the voltage limit signal, the desired delivery current signal and the second power limit signal in response to one of the current state signal and the power state signal.

9. The operable iontophoretic drug delivery system of one of claims 6-8 wherein the electronic circuit further comprises:

output enable switch means (74), the output enable switch means (74) being coupled to the circuit in series between one of the electrodes (22,25) of the drug delivery device (20) and the voltage and current generating means (68,70), the output enable switch means (74) being responsive to a dose state signal and selectively interrupting current flow provided to said one of the electrodes (22,25) in response thereto,

total drug dose sensing means (76), the total drug dose sensing means (76) receiving a predetermined total dose signal and comparing the total dose signal with a signal substantially representative of the quantity of drug administered to the patient by the drug delivery device (20) and generating the dose state signal in response to the comparison thereof, and

means (84) for determining the quantity of current over time provided to the electrodes (22,25) of the drug delivery device (20), the current quantity determining means (84) providing an accumulated current signal in response thereto, the accumulated current signal being the signal substantially representative of the quantity of drug administered to the patient by the drug delivery device (20).

10. The operable iontophoretic drug delivery system of one of claims 6-9 wherein the electronic circuit further comprises:

output enable switch means (74), the output enable switch means (74) being coupled to the circuit in series between one of the electrodes (22,25) of the drug delivery device (20) and the voltage and current generating means (68,70), the output enable switch means (74) being responsive to an excess current limit signal and selectively interrupting current flow provided to said one of the electrodes (22,25) in response thereto, and

means (82) for comparing the sensed current feedback signal with a predetermined excess current threshold signal and generating the excess current limit signal in response to the comparison thereof.

11. The operable iontophoretic drug delivery system of claim 1 wherein the circuit means comprise a biphasic power source (81,83) connected to the first and second electrodes (22,25) of the drug delivery device (20), the biphasic

power source (81,83) including means for providing a constant voltage, and means for providing a constant current, the biphasic power source (81,83) being in a first mode and supplying a constant voltage to the first and second electrodes (22,25) when the skin impedance of the animal is at least equal to a predetermined level, and wherein the biphasic power source (81,83) is in a second mode and supplying a constant current to the first and second electrodes when the skin impedance of the animal is less than the predetermined level.

12. The operable iontophoretic drug delivery system of claim 11 wherein the constant voltage means is a zener diode (85) which limits the voltage across the first and second electrodes (22,25) to between about 3 V and about 30 V and preferably to between about 6 V and about 20 V.

13. The operable drug delivery system of claim 1, wherein the circuit means is an electrical control circuit and wherein said switching means includes power limiting means for causing a transition from one of said constant voltage and constant current to a constant power provided to the electrodes (22,25) if a predetermined power between said electrodes is reached.

14. A method for iontophoretic drug delivery through the skin of an animal not directed to the treatment of the animal body by therapy, using an iontophoretic drug delivery device (20) having an ionic compound containing reservoir (21), a first electrode (22) in said ionic compound containing reservoir (21), and a second electrode (25), comprising the steps of:

- attaching said iontophoretic drug delivery device (20) to the skin of an animal, and
- causing electrical power to flow between said electrodes (22,25), characterized in that
- in a first mode, when the device is activated the electrical power is caused to flow between said electrodes (22,25) at a constant predetermined voltage,
- the current is monitored while said power is being delivered at constant voltage,
- the electrical power between said electrodes (22,25) is caused to change from the first mode to a second mode wherein constant current is provided, when said monitored current reaches a predetermined current,
- in the second mode the electrical power is continuously caused to flow between said electrodes (22,25) at a constant predetermined current, the drug delivery device having an electrolyte containing reservoir (23), said second electrode (25) being disposed in said electrolyte containing reservoir (23).

15. The method for iontophoretic drug delivery of claim 14, the method comprising a power control routine when the power is caused to flow at a constant current, the current being monitored, the power control routine comprising the steps of:

monitoring the power between said electrodes (22,25), and

if the monitored power reaches a predetermined value, causing the electrical power to be changed from one of constant voltage and constant current to a constant power provided to the electrodes (22,25) when a predetermined power provided to the electrodes (22,25) is reached, the method further comprising a terminating routine, the terminating routine comprising the steps of:

monitoring and accumulating the total current passing between said electrodes (22,25), and

terminating electrical power provided to said electrodes (22,25) when the accumulated total amount of current, corresponding the delivery of the desired amount of ionic compound into the skin of the animal, has been reached.

## Patentansprüche

1. Betreibbares Ionotophoresemedikamentenzufuhrsystem mit einem Medikamentenreservoir (21), das an der Haut eines Säugetiers angebracht werden kann, einer ersten Elektrode (22) in dem Medikamentenreservoir (21), einer

zweiten Elektrode (25), die mit dem Säugetier in elektrischen Kontakt gebracht werden kann, einer Schaltungseinrichtung, die eine elektrische Verbindung zwischen den ersten und zweiten Elektroden (22, 25) herstellt, wobei die Schaltungseinrichtung eine Einrichtung zum Anschließen an eine elektrische Stromquelle aufweist, wobei die Schaltungseinrichtung eine Versorgungseinrichtung aufweist, die einer der Elektroden (22) einen gesteuerten konstanten Strom zuführt,

gekennzeichnet durch

ein Elektrolytreservoir (23), das mit der Haut des Säugetiers in Verbindung gebracht werden kann, wobei die zweite Elektrode (25) in dem Elektrolytreservoir angeordnet ist, wobei die Schaltungseinrichtung ferner eine erste Versorgungseinrichtung aufweist, die eine gesteuerte konstante Spannung zwischen den Elektroden (22, 25) liefert, wenn die Vorrichtung eingeschaltet ist, wobei die Schaltungseinrichtung eine Einrichtung zum Überwachen eines Stroms durch eine der beiden Elektroden (22) und eine Umschalteneinrichtung in der Schaltungseinrichtung aufweist, die von einem ersten Modus umschaltet, in dem die erste Versorgungseinrichtung eine konstante Spannung liefert, zu einem zweiten Modus, in dem eine zweite Versorgungseinrichtung einen konstanten Strom liefert, wenn der durch die Überwachungseinrichtung überwachte Strom eine vorbestimmte Stärke erreicht.

2. Betreibbares Ionotopharesemedikamentenzufuhrsystem nach Anspruch 1, wobei das Medikamentenreservoir (21) eine Ionenverbindung enthält, die aus der Gruppe therapeutischer Verbindungen, diagnostischer Verbindungen und Medikamenten ausgewählt ist, und wobei die erste Elektrode (22) ein leitendes Element aufweist, das aus der Gruppe ausgewählt ist, die Silber, Silber/Chlorid, Gold, Kupfer, Molybdän und Blei enthält.

3. Betreibbares Ionotopharesemedikamentenzufuhrsystem nach Anspruch 1 oder 2, ferner mit einer Strombegrenzungseinrichtung in der Umschalteneinrichtung, die einen Übergang von entweder einer konstanten Spannung oder einem konstanten Strom zu einer konstanten Leistung bewirkt, die an die ersten und zweiten Elektroden (22, 25) geliefert wird, wenn eine vorbestimmte Leistung erreicht ist.

4. Betreibbares Ionotopharesemedikamentenzufuhrsystem nach einem der Ansprüche 1-3, mit einer Einrichtung zum Messen des durch die erste Elektrode (22) fließenden Stroms und zum Akkumulieren des durch die erste Elektrode fließenden Gesamtstroms.

5. Betreibbares Ionotopharesemedikamentenzufuhrsystem nach Anspruch 4, mit einer Einrichtung zum Unterbrechen der Leistungszufuhr zu der ersten Elektrode (22), wenn der akkumulierte Gesamtstrom eine vorbestimmte Stärke erreicht.

6. Betreibbares Ionotopharesemedikamentenzufuhrsystem nach einem der Ansprüche 1-5, wobei die Schaltungseinrichtung eine elektronische Schaltung enthält, die folgendes aufweist:

eine einstellbare Spannungs- und Stromerzeugungseinrichtung (68, 70), die mit den Elektroden (22, 25) der Medikamentenzufuhrvorrichtung (20) verbunden ist und entweder einen selektiv einstellbaren Strom oder eine selektiv einstellbare Spannung an die Elektroden (22, 25) liefert,

eine Einrichtung zum Detektieren des an die Elektroden (22, 25) der Medikamentenzufuhrvorrichtung (20) gelieferten Stroms (56, 58), wobei die Stromdetektionseinrichtung (56, 58) ein Rückkopplungssignal des detektierten Stroms erzeugt, das proportional zu dem detektierten Elektrodenstrom ist,

eine Einrichtung (54) zum Detektieren der an die Elektroden der Medikamentenzufuhrvorrichtung (20) gelieferten Spannung, wobei die Spannungsdetektionseinrichtung (54) ein Rückkopplungssignal der detektierten Spannung erzeugt, das proportional zu der detektierten Elektrodenspannung ist,

eine mit der Stromdetektionseinrichtung (56, 58) verbundene Einrichtung (64) zum Vergleichen des Rückkopplungssignals des detektierten Stroms mit einem vorbestimmten Stromschwellwertsignal und zum Erzeugen eines Stromzustandssignals als Reaktion auf den Vergleich,

eine Rückkopplungssignalauswahleinrichtung (52), die wenigstens auf das Stromzustandssignal reagiert und wenigstens das Rückkopplungssignal des detektierten Stroms und das Rückkopplungssignal der detektierten Spannung empfängt und als Reaktion auf wenigstens das Spannungszustandssignal ein Rückkopplungssignal erzeugt, das wenigstens entweder dem Rückkopplungssignal des detektierten Stroms oder dem Rückkopplungssignal der detektierten Spannung entspricht,

eine Sollwertauswahleinrichtung (50), die ein vorausgewähltes Spannungsgrenzsignal und ein vorausgewähltes gewünschtes Medikamentenzufuhrstromsignal empfängt und auf wenigstens das Stromzustandssignal reagiert, wobei die Sollwertauswahleinrichtung (50) als Reaktion auf wenigstens das Stromzustandssignal ein Sollwertsignal erzeugt, das wenigstens entweder dem Spannungsgrenzsignal oder dem gewünschten Zufuhrstromsignal entspricht,

eine Einrichtung (53) zur Subtraktion des Rückkopplungssignals von dem Sollwertsignal, wobei die Subtraktionseinrichtung ein Ehlersignal erzeugt, das der Differenz zwischen dem Rückkopplungssignal und dem Sollwertsignal entspricht, und

die Spannungs- und Stromerzeugungseinrichtung (68, 70) auf das Ehlersignal reagiert und als Reaktion hierauf wenigstens entweder den an die Elektroden (22, 25) gelieferten Strom oder die an die Elektroden (22, 25) gelieferte Spannung einstellen.

7. Betreibbares Ionotopharesemedikamentenzufuhrsystem nach Anspruch 6, wobei die einstellbare Spannungs- und Stromerzeugungseinrichtung (68, 70) einen variablen Impulsgenerator (68) und einen mit dem variablen Impulsgenerator (68) verbundenen Impuls-Leistungs-Konverter (70) aufweist, wobei der variable Impulsgenerator (68) auf das Ehlersignal reagiert und ein pulsierendes Ausgangssignal erzeugt, das dem Ehlersignal entsprechend variiert, wobei der Impuls-Leistungs-Konverter (70) auf das Ausgangssignal des variablen Impulsgenerators (68) reagiert und eine Ausgangsspannung erzeugt, die entsprechend dem Ausgangssignal des Impulsgenerators (68) variiert.

8. Betreibbares Ionotopharesemedikamentenzufuhrsystem nach Anspruch 6 oder 7, wobei die elektronische Schaltung ferner aufweist:

eine Multiplikationseinrichtung (60), die das Rückkopplungssignal des detektierten Stroms und das Rückkopplungssignal der detektierten Spannung empfängt und das Rückkopplungssignal des detektierten Stroms und das Rückkopplungssignal der detektierten Spannung effektiv miteinander multipliziert und als Reaktion auf die Multiplikation ein Rückkopplungssignal einer detektierten Leistung erzeugt, wobei das Rückkopplungssignal der detektierten Leistung an die Rückkopplungssignalauswahleinrichtung (52) übermittelt wird, und

eine mit der Multiplikationseinrichtung (60) verbundene Einrichtung (66) zum Vergleichen des Rückkopplungssignals der detektierten Leistung mit einem vorbestimmten ersten Leistungsgrenzsignal und Erzeugen eines Leistungszustandssignals als Reaktion auf den Vergleich,

wobei die Rückkopplungssignalauswahleinrichtung (52) entweder auf das Stromzustandssignal oder das Leistungszustandssignal reagiert, wobei das von der Rückkopplungssignalauswahleinrichtung (52) erzeugte Rückkopplungssignal als Reaktion auf entweder das Stromzustandssignal oder das Leistungszustandssignal entweder dem Rückkopplungssignal der detektierten Strom oder dem Rückkopplungssignal des detektierten Stroms oder dem Rückkopplungssignal der detektierten Leistung entspricht, und

wobei ein vorbestimmtes zweites Leistungsgrenzsignal an die Sollwertauswahleinrichtung (50) geliefert wird, die entweder auf das Stromzustandssignal oder das Leistungszustandssignal reagiert, wobei das durch die Sollwertauswahleinrichtung (50) erzeugte Sollwertsignal als Reaktion auf entweder das Stromzustandssignal oder das Leistungszustandssignal entweder dem Spannungsgrenzsignal oder dem gewünschten Zufuhrstromsignal oder dem zweiten Leistungsgrenzsignal entspricht.

9. Betreibbares Ionotopharesemedikamentenzufuhrsystem nach einem der Ansprüche 6-8, wobei die elektronische Schaltung folgendes aufweist:

eine Ausgangsfreigabeumschalteneinrichtung (74), die mit der Schaltung zwischen einer der Elektroden (22, 25) der Medikamentenzufuhrvorrichtung (20) und der Spannungs- und Stromerzeugungseinrichtung (68, 70) in Reihe geschaltet ist, wobei die Ausgangsfreigabeumschalteneinrichtung (74) auf ein Dosiszustandssignal reagiert und als Reaktion hierauf selektiv den an eine der Elektroden (22, 25) gelieferten Stromfluß unterbricht,

eine Gesamtmedikamentendosisdetektionseinrichtung (76), die ein vorbestimmtes Gesamtdosisignal empfängt und das Gesamtdosisignal mit einem Signal vergleicht, das im wesentlichen die dem Patienten durch die Medikamentenzufuhrvorrichtung (20) verabreichte Medikamentenmenge darstellt und als Reaktion auf den Vergleich ein Dosiszustandssignal erzeugt, und

eine Einrichtung (84) zum Bestimmen des über einen Zeitraum an die Elektroden (22, 25) der Medikamentenzufuhrvorrichtung (20) gelieferten Stroms, wobei die Strombestimmungseinrichtung (84) als Reaktion ein akkumuliertes Stromsignal liefert, welches das Signal ist, das im wesentlichen die dem Patienten durch die Medikamentenzufuhrvorrichtung (20) verabreichte Medikamentenmenge darstellt.

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10. Betreibbares Ionotopharesemedikamentenzufuhrsystem nach einem der Ansprüche 6-9, wobei die elektronische Schaltung folgendes aufweist:

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eine Ausgangsfreigabeumschalteneinrichtung (74), die mit der Schaltung zwischen einer der Elektroden (22, 25) der Medikamentenzufuhrvorrichtung (20) und der Spannungs- und Stromerzeugungseinrichtung (68, 70) in Reihe geschaltet ist, wobei die Ausgangsfreigabeumschalteneinrichtung (74) auf ein Überschußstromgrenzsignal reagiert und als Reaktion auf den Vergleich selektiv den an eine der Elektroden (22, 25) gelieferten Stromfluß unterbricht, und

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eine Einrichtung (82) zum Vergleichen des Rückkopplungssignals des detektierten Stroms mit einem vorbestimmten Überschußstromschwellwertsignal und zum Erzeugen des Überschußstromgrenzsignal als Reaktion auf den Vergleich.

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11. Betreibbares Ionotopharesemedikamentenzufuhrsystem nach Anspruch 1, wobei die Schaltungseinrichtung eine mit den ersten und zweiten Elektroden (22, 25) der Medikamentenzufuhrvorrichtung verbundene Zweiphasenstromquelle (81, 83) aufweist, die eine Einrichtung zum Liefern einer konstanten Spannung und eine Einrichtung zum Liefern eines konstanten Stroms aufweist, wobei die Zweiphasenstromquelle (81, 83) in einem ersten Modus ist und den ersten und zweiten Elektroden (22, 25) eine konstante Spannung zuführt, wenn die Hautimpedanz des Säugetiers wenigstens gleich einer vorbestimmten Stärke ist, und wobei die Zweiphasenstromquelle (81, 83) in einem zweiten Modus ist und den ersten und zweiten Elektroden einen konstanten Strom zuführt, wenn die Hautimpedanz des Säugetiers weniger als die vorbestimmte Stärke aufweist.

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12. Betreibbares Ionotopharesemedikamentenzufuhrsystem nach Anspruch 11, wobei die Konstantspannungseinrichtung eine Zener-Diode (85) ist, die die Spannung an den ersten und zweiten Elektroden (22, 25) auf zwischen etwa 3 V und etwa 30 V und vorzugsweise auf zwischen etwa 6 V und etwa 20 V begrenzt.

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13. Betreibbares Ionotopharesemedikamentenzufuhrsystem nach Anspruch 1, wobei die Schaltungseinrichtung eine elektrische Steuerschaltung ist und wobei die Umschalteneinrichtung eine Leistungsbegrenzungseinrichtung aufweist, die einen Übergang von entweder einer konstanten Spannung oder einem konstanten Strom zu einer konstanten Leistung bewirkt, die an die ersten und zweiten Elektroden (22, 25) geliefert wird, wenn eine vorbestimmte Leistung zwischen den Elektroden erreicht ist.

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14. Verfahren zur Ionotopharesemedikamentenzufuhr durch die Haut eines Säugetiers, die nicht auf die Behandlung des Säugetierkörpers durch Therapie gerichtet ist, unter Verwendung einer Ionotopharesemedikamentenzufuhrvorrichtung (20) mit einem eine Ionenverbindung enthaltenden Reservoir (21), einer ersten Elektrode (22) in dem die Ionenverbindung enthaltenden Reservoir (21) und einer zweiten Elektrode, mit folgenden Schritten:

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- Anbringen der Ionotopharesemedikamentenzufuhrvorrichtung (20) an der Haut eines Säugetiers, und
- Erzeugen einer elektrischen Leistung zwischen den Elektroden (22, 25);  
dadurch gekennzeichnet, daß
- bei einem ersten Modus, wenn die Vorrichtung eingeschaltet ist, bewirkt wird, daß die elektrische Leistung zwischen den Elektroden (22, 25) mit einer konstanten vorbestimmten Spannung fließt,
- die Strom überwacht wird, während die Leistung mit einer konstanten Spannung zugeführt wird,
- bewirkt wird, daß die elektrische Leistung zwischen den Elektroden (22, 25) sich von dem ersten Modus zu einem zweiten Modus ändert, wobei ein konstanter Strom vorgesehen ist, wenn der überwachte Strom einen vorbestimmten Strom erreicht,
- in dem zweiten Modus kontinuierlich bewirkt wird, daß die elektrische Leistung mit einem konstanten vorbestimmten Strom zwischen den Elektroden (22, 25) anliegt, wobei die Medikamentenzufuhrvorrichtung ein ein

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Elektrolyt enthaltendes Reservoir (23) aufweist, wobei die zweite Elektrode (25) in dem das Elektrolyt enthaltenden Reservoir (23) vorgesehen ist.

15. Verfahren zur Ionophoresemedikamentenzufuhr nach Anspruch 14, wobei das Verfahren eine Leistungssteuerroutine aufweist, wobei der Strom überwacht wird, wenn die Leistung mit einem konstanten Strom angelegt wird, wobei die Leistungssteuerroutine folgende Schritte aufweist:

Überwachen der Leistung zwischen den Elektroden (22, 25), und,

Ändern der elektrischen Leistung von entweder einer konstanten Spannung oder einem konstanten Strom zu einer an die Elektroden (22, 25) gelieferten konstanten Leistung, wenn die überwachte Leistung eine vorbestimmte Stärke erreicht und eine vorbestimmte an die Elektroden (22, 25) gelieferte Leistung erreicht wird, wobei das Verfahren ferner eine Abschaltoutine mit folgenden Schritten aufweist:

Überwachen und Akkumulieren des zwischen den Elektroden (22, 25) fließenden Gesamtstroms, und

Abschalten der an die Elektroden (22, 25) gelieferten elektrischen Leistung, wenn die akkumulierte Gesamtmenge des Stroms, die der Zufuhr der gewünschten Menge der Ionenverbindung in die Haut des Säugetiers entspricht, erreicht ist.

## Revendications

1. Dispositif d'administration de médicament par ionophorèse réglable, comprenant un réservoir de médicament (21) conçu pour être fixé sur la peau d'un animal, une première électrode (22) dans ledit réservoir de médicament (21), une seconde électrode (25) conçue pour être portée en contact électrique avec ledit animal, un moyen formant circuit destiné à assurer une communication électrique entre lesdites première et seconde électrodes (22, 25), ledit moyen formant circuit comprenant un moyen de connexion à une source de puissance électrique, ledit moyen formant circuit comprenant un moyen d'alimentation destiné à délivrer un courant constant commandé à l'une desdites électrodes (22), caractérisé par:
  - un réservoir d'électrolyte (23) adapté pour être placé en communication avec la peau dudit animal, ladite seconde électrode (25) étant positionnée à l'intérieur dudit réservoir d'électrolyte, ledit moyen formant circuit comprenant, en outre, un premier moyen d'alimentation destiné à délivrer une tension constante commandée entre lesdites électrodes (22, 25) lorsque le dispositif est activé, ledit moyen formant circuit comprenant un moyen destiné à surveiller le courant à travers l'une desdites électrodes (22), et un moyen de commutation, dans ledit moyen formant circuit, destiné à basculer d'un premier mode dans lequel ledit premier moyen d'alimentation délivre une tension constante à un second mode dans lequel un second moyen d'alimentation délivre un courant constant, lorsque ledit courant surveillé par ledit moyen de surveillance atteint une valeur prédéterminée.
2. Dispositif d'administration de médicament par ionophorèse réglable selon la revendication 1, dans lequel ledit réservoir de médicament (21) contient un composé ionique sélectionné à partir du groupe consistant en composés thérapeutiques, composés de diagnostics et médicaments, et dans lequel ladite première électrode (22) comprend un élément conducteur sélectionné à partir du groupe consistant en l'argent, l'argent/chlorure, l'or, le cuivre, le molybdène et le plomb.
3. Dispositif d'administration de médicament par ionophorèse réglable selon la revendication 1 ou 2, comprenant, en outre, un moyen de limitation de puissance, dans ledit moyen de commutation, afin de provoquer une transition à partir d'un mode à tension constante et à courant constant vers un mode à puissance constante délivrée aux première et seconde électrodes (22, 25) si une puissance prédéterminée est atteinte.
4. Dispositif d'administration de médicament par ionophorèse réglable selon l'une des revendications 1 à 3, comprenant, en outre, un moyen destiné à mesurer le courant passant à travers ladite première électrode (22) et à cumuler le courant total passant à travers ladite première électrode.
5. Dispositif d'administration de médicament par ionophorèse réglable selon la revendication 4, comprenant, en outre, un moyen destiné à couper la puissance sur ladite première électrode (22) lorsque le courant total cumulé atteint une valeur prédéterminée.

6. Dispositif d'administration de médicament par ionophorèse réglable selon l'une des revendications 1 à 5, dans lequel le moyen formant circuit est constitué par un circuit électronique, ledit circuit électronique comprenant:

un moyen de production de tension et de courant réglables (68, 70) couplé aux électrodes (22, 25) du dispositif d'administration de médicament (20) et délivrant l'un d'un courant et d'une tension réglables de manière sélective sur les électrodes (22, 25),  
 un moyen destiné à détecter le courant (56, 58) délivré aux électrodes (22, 25) du dispositif d'administration de médicament (20), le moyen de détection de courant (56, 58) produisant un signal d'asservissement de courant détecté qui est proportionnel au courant d'électrode détecté,  
 un moyen (54) destiné à détecter la tension délivrée aux électrodes du dispositif d'administration de médicament (20), le moyen de détection de tension (54) produisant un signal d'asservissement de tension détectée qui est proportionnel à la tension d'électrode détectée,  
 un moyen (64) couplé au moyen de détection de courant (56, 58) afin de comparer le signal d'asservissement de courant détecté avec un signal de seuil de courant prédéterminé et à produire un signal d'état de courant en fonction de leur comparaison,  
 un moyen de sélection de signal d'asservissement (52), le moyen de sélection de signal d'asservissement (52) étant sensible au moins au signal d'état de courant et recevant au moins le signal d'asservissement de courant détecté et le signal d'asservissement de tension détectée et produisant un signal d'asservissement correspondant à au moins l'un du signal d'asservissement de courant détecté et du signal d'asservissement de tension détectée au moins en fonction du signal d'état de courant,  
 un moyen de sélection de point de consigne (50), le moyen de sélection de point de consigne (50) recevant un signal de limite de tension présélectionné et un signal de courant d'administration de médicament désiré présélectionné et étant sensible au moins au signal d'état de courant, le moyen de sélection de point de consigne (50) produisant un signal de consigne correspondant à au moins l'un du signal de limite de tension et du signal de courant d'administration désiré au moins en fonction du signal d'état de courant,  
 un moyen (53) destiné à soustraire le signal d'asservissement du signal de consigne, le moyen de soustraction produisant un signal d'erreur correspondant à la différence entre le signal d'asservissement et le signal de consigne, et  
 le moyen de production de tension et de courant (68, 70) étant sensible au signal d'erreur et réalisant le réglage d'au moins l'un du courant et de la tension délivrés aux électrodes (22, 25) en fonction celui-ci.

7. Dispositif d'administration de médicament par ionophorèse réglable selon la revendication 6, dans lequel le moyen de production de tension et de courant réglables (68, 70) comprend un générateur d'impulsion variable (68) et un convertisseur d'impulsion en puissance (70) couplé au générateur d'impulsion variable (68), le générateur d'impulsion variable (68) étant sensible au signal d'erreur et produisant un signal de sortie impulsionnel qui varie en fonction du signal d'erreur, le convertisseur d'impulsion en puissance (70) étant sensible au signal de sortie du générateur d'impulsion variable (68) et produisant une tension de sortie qui varie en fonction du signal de sortie du générateur d'impulsion (68).

8. Dispositif d'administration de médicament par ionophorèse réglable selon la revendication 6 ou 7, dans lequel le circuit électronique comprend, en outre:

un moyen de multiplication (60), le moyen de multiplication recevant le signal d'asservissement de courant détecté et le signal d'asservissement de tension détectée et multipliant la valeur efficace du signal d'asservissement de courant détecté et du signal d'asservissement de tension détectée ensemble et produisant un signal d'asservissement de puissance détectée en fonction de leur produit, le signal d'asservissement de puissance détectée étant délivré au moyen de sélection de signal d'asservissement (52), et  
 un moyen (66) couplé au moyen de multiplication (60) destiné à comparer le signal d'asservissement de puissance détectée avec un premier signal de limite de puissance prédéterminé et à produire un signal d'état de puissance en réponse à leur comparaison,  
 dans lequel le moyen de sélection de signal d'asservissement (52) est sensible à l'un du signal d'état de courant et du signal d'état de puissance, le signal d'asservissement produit par le moyen de sélection de signal d'asservissement (52) correspondant à l'un du signal d'asservissement de courant détecté, du signal d'asservissement de tension détectée et du signal d'asservissement de puissance détectée en fonction de l'un du signal d'état de courant et du signal d'état de puissance, et  
 dans lequel un second signal de limite de puissance présélectionné est délivré au moyen de sélection de point de consigne (50), le moyen de sélection de point de consigne (50) étant sensible à l'un du signal d'état de courant et du signal d'état de puissance, le signal de consigne produit par le moyen de sélection de point

de consigne (50) correspondant à l'un du signal de limite de tension, du signal de courant d'administration désiré et du second signal de limite de puissance en fonction de l'un du signal d'état de courant et du signal d'état de puissance.

9. Dispositif d'administration de médicament par ionophorèse réglable selon l'une des revendications 6 à 8, dans lequel le circuit électronique comprend, en outre:

un moyen de commutation de validation de sortie (74), le moyen de commutation de validation de sortie (74) étant couplé au circuit, en série entre l'une des électrodes (22, 25) du dispositif d'administration de médicament (20) et le moyen de production de tension et de courant (68, 70), le moyen de commutation de validation de sortie (74) étant sensible à un signal d'état de dose et interrompant de manière sélective le passage du courant délivré à ladite une des électrodes (22, 25) en fonction de celui-ci,

un moyen de détection de dose totale de médicament (76), le moyen de détection de dose totale de médicament (76) recevant un signal de dose totale prédéterminé et comparant le signal de dose totale avec un signal sensiblement représentatif de la quantité de médicament administrée au patient par le dispositif d'administration de médicament (20) et produisant le signal d'état de dose en fonction de leur comparaison, et

un moyen (84) destiné à déterminer la quantité de courant en fonction du temps délivré aux électrodes (22, 25) du dispositif d'administration de médicament (20), le moyen de détermination de quantité de courant (84) délivrant un signal de courant cumulé en fonction de celle-ci, le signal de courant cumulé étant le signal sensiblement représentatif de la quantité de médicament administrée au patient par le dispositif d'administration de médicament (20).

10. Dispositif d'administration de médicament par ionophorèse réglable selon l'une des revendications 6 à 9, dans lequel le circuit électronique comprend, en outre:

un moyen de commutation de validation de sortie (74), le moyen de commutation de validation de sortie (74) étant couplé au circuit, en série entre l'une des électrodes (22, 25) du dispositif d'administration de médicament (20) et le moyen de production de tension et de courant (68, 70), le moyen de commutation de validation de sortie (74) étant sensible à un signal de limite d'excès de courant et interrompant de manière sélective le passage du courant délivré à l'une desdites électrodes (22, 25) en fonction de celui-ci, et

un moyen (82) destiné à comparer le signal d'asservissement de courant détecté avec un signal de seuil d'excès de courant prédéterminé et produisant le signal de limite d'excès de courant en fonction de leur comparaison.

11. Dispositif d'administration de médicament par ionophorèse réglable selon la revendication 1, dans lequel le moyen formant circuit comprend une source de puissance diphasée (81, 83) connectée aux première et seconde électrodes (22, 25) du dispositif d'administration de médicament (20), la source de puissance diphasée (81, 83) comprenant un moyen destiné à produire une tension constante, et un moyen destiné à produire un courant constant, la source de puissance diphasée (81, 83) étant dans un premier mode et délivrant une tension constante aux première et seconde électrodes (22, 25) lorsque l'impédance de peau de l'animal est au moins égale à une valeur prédéterminée, et dans lequel la source de puissance diphasée (81, 83) est dans un second mode et délivre un courant constant aux première et seconde électrodes lorsque l'impédance de peau de l'animal est inférieure à une valeur prédéterminée.

12. Dispositif d'administration de médicament par ionophorèse réglable selon la revendication 11, dans lequel le moyen délivrant une tension constante est une diode Zener (85) qui limite la tension entre les première et seconde électrodes (22, 25) à une valeur située entre 3 V environ et 30 V environ et, de préférence, entre 6 V environ et 20 V environ.

13. Dispositif d'administration de médicament réglable selon la revendication 1, dans lequel le moyen formant circuit est un circuit de commande électrique et dans lequel ledit moyen de commutation comprend un moyen de limitation de puissance destiné à provoquer une transition entre l'un desdits modes à tension constante et à courant constant vers un mode à puissance constante délivrée aux électrodes (22, 25) si une puissance prédéterminée entre lesdites électrodes est atteinte.

14. Procédé d'administration de médicament par ionophorèse à travers la peau d'un animal et destiné au traitement du corps de l'animal par thérapie, en utilisant un dispositif d'administration de médicament par ionophorèse (20) comprenant un réservoir (21) contenant un composé ionique, une première électrode (22) dans ledit réservoir (21) con-

tenant un composé ionique et une seconde électrode (25), comprenant les étapes de:

fixation dudit dispositif d'administration de médicament par ionophorèse (20) sur la peau d'un animal, et établissement du passage de puissance électrique entre lesdites électrodes (22, 25),

caractérisé en ce que:

dans un premier mode, lorsque le dispositif est activé, la fourniture de la puissance électrique est établie entre lesdites électrodes (22, 25) sous une tension prédéterminée constante, le courant est surveillé pendant la fourniture de ladite puissance sous une tension constante, la fourniture de puissance électrique entre lesdites électrodes (22, 25) est modifiée à partir du premier mode vers un second mode dans lequel un courant constant est délivré, lorsque ledit courant surveillé atteint un courant prédéterminé,

dans le second mode, la puissance électrique est fournie de manière continue entre lesdites électrodes (22, 25) sous un courant constant prédéterminé, le dispositif d'administration de médicament comprenant un réservoir (23) contenant un électrolyte, ladite seconde électrode (25) étant disposée dans ledit réservoir (23) contenant de l'électrolyte.

15. Procédé d'administration de médicament par ionophorèse selon la revendication 14, le procédé comprenant un programme de commande de puissance s'exécutant pendant la fourniture de la puissance sous un courant constant, le courant étant surveillé, le programme de commande de puissance comprenant les étapes de:

surveillance de la puissance entre lesdites électrodes (22, 25), et

si la puissance surveillée atteint une valeur prédéterminée, de modification de la fourniture de puissance électrique délivrée aux électrodes (22, 25) à partir d'un mode à tension constante et à courant constant vers un mode à puissance constante, lorsqu'une puissance prédéterminée délivrée aux électrodes (22, 25) est atteinte, le procédé comprenant, en outre, un sous-programme d'achèvement, le sous-programme d'achèvement comprenant les étapes de:

surveillance et calcul du courant total cumulé passant entre lesdites électrodes (22, 25), et arrêt de la fourniture de la puissance électrique auxdites électrodes (22, 25) lorsque la quantité totale cumulée du courant, correspondant à l'administration de la quantité désirée de composé ionique dans la peau de l'animal, a été atteinte.

FIG-1

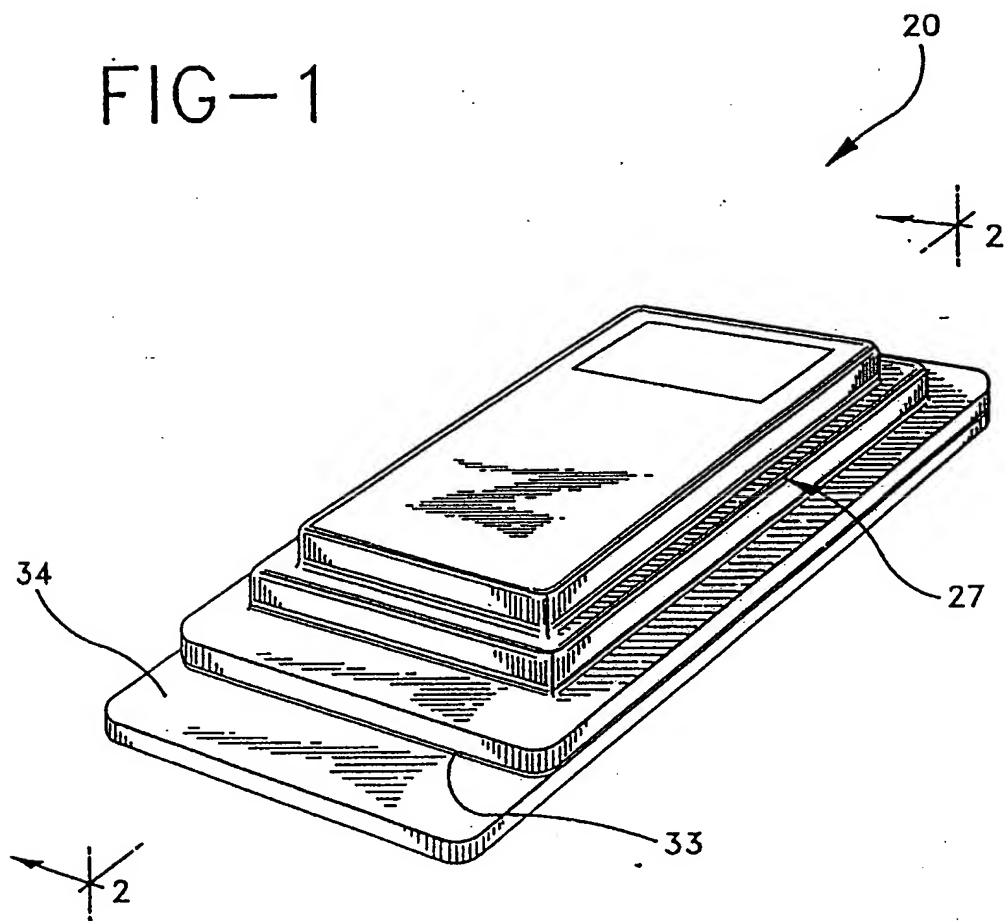


FIG-2

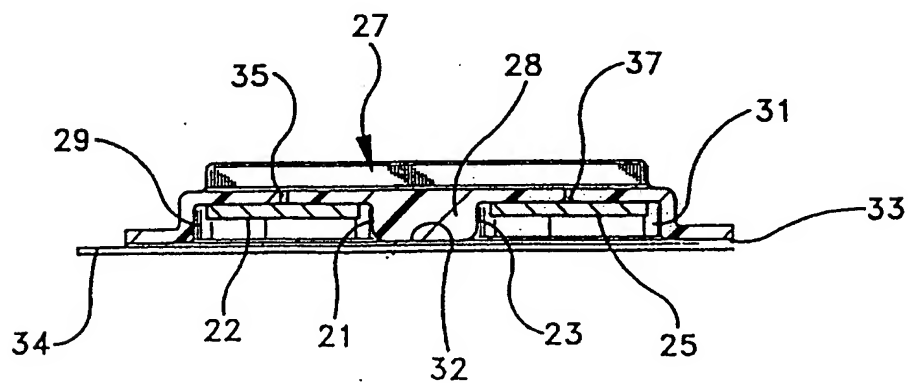


FIG-3

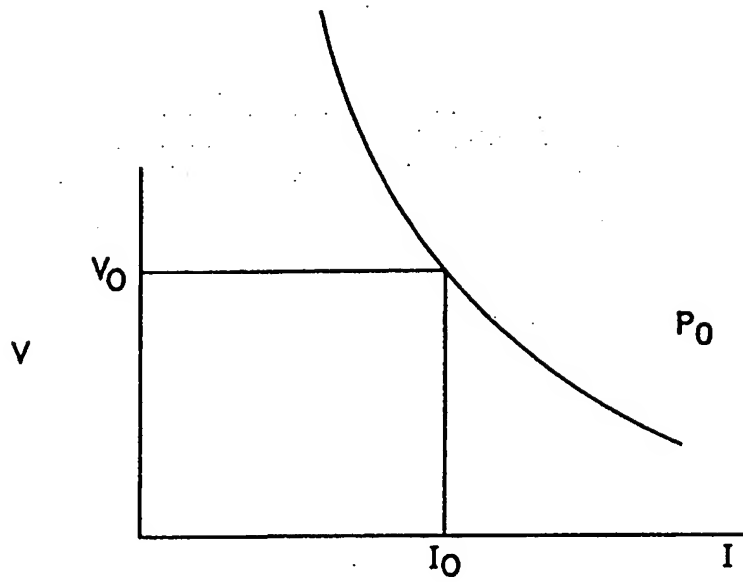
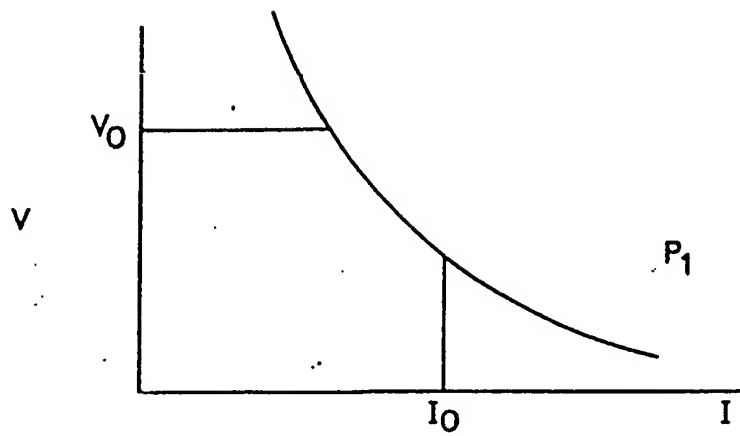
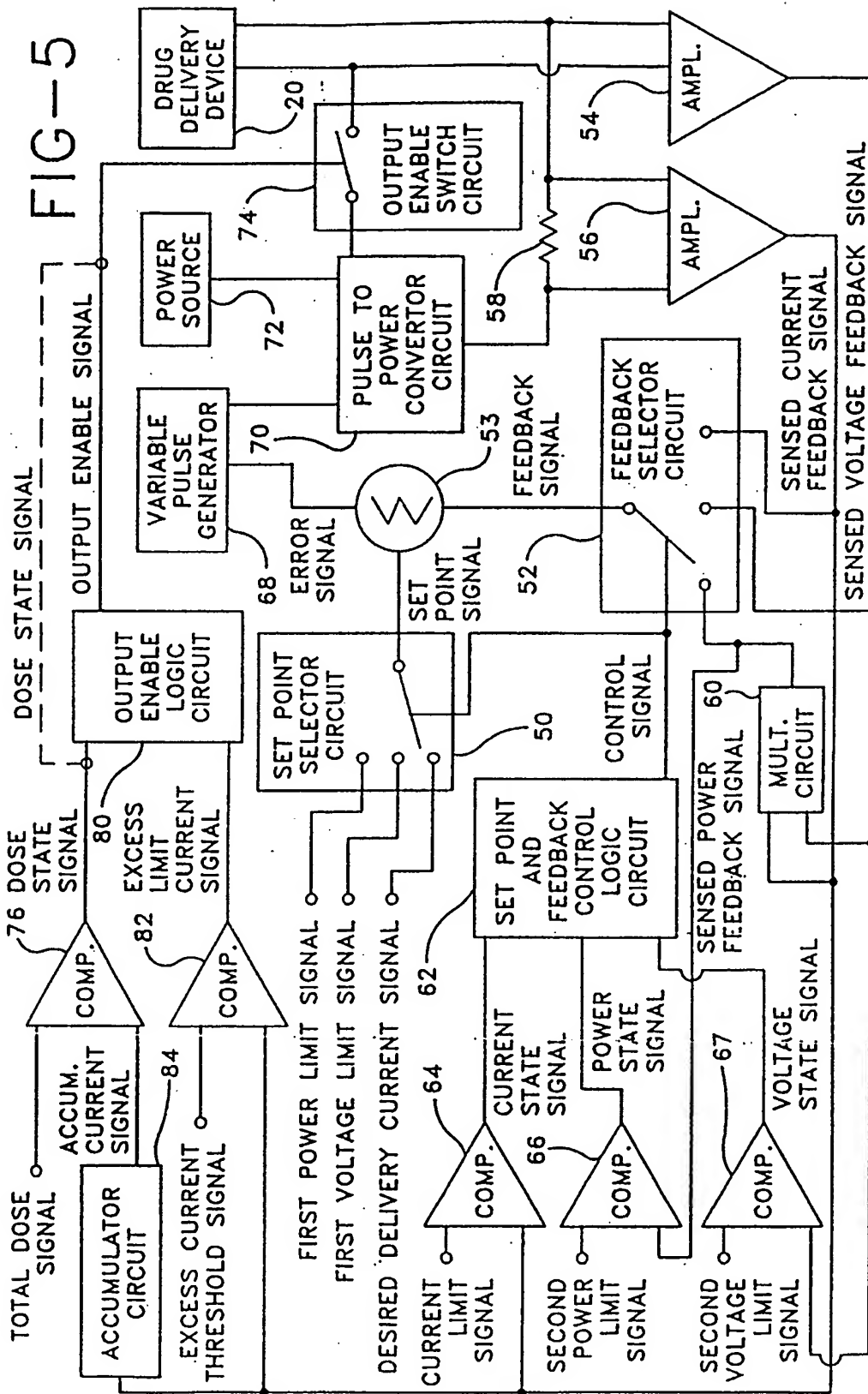
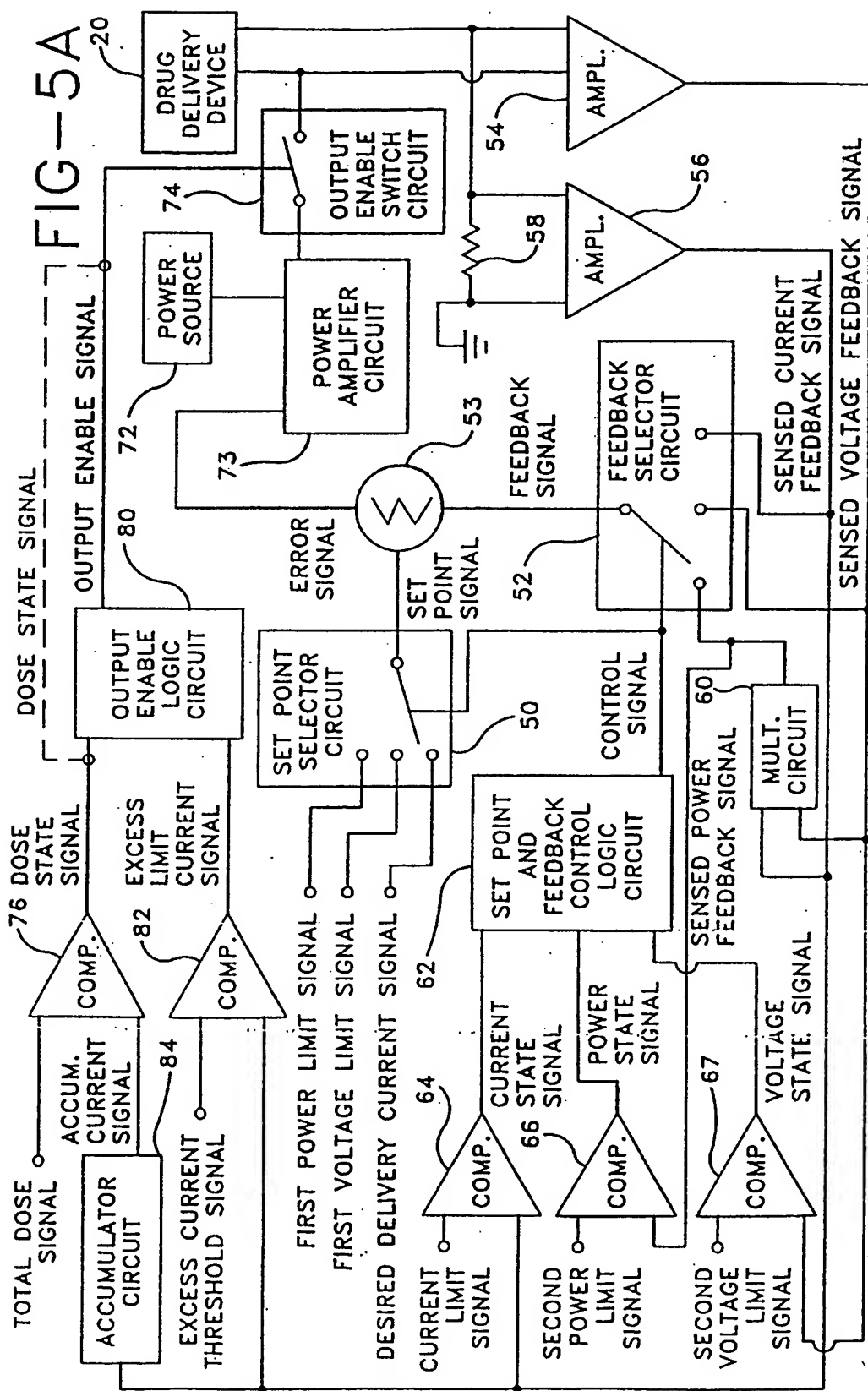


FIG-4







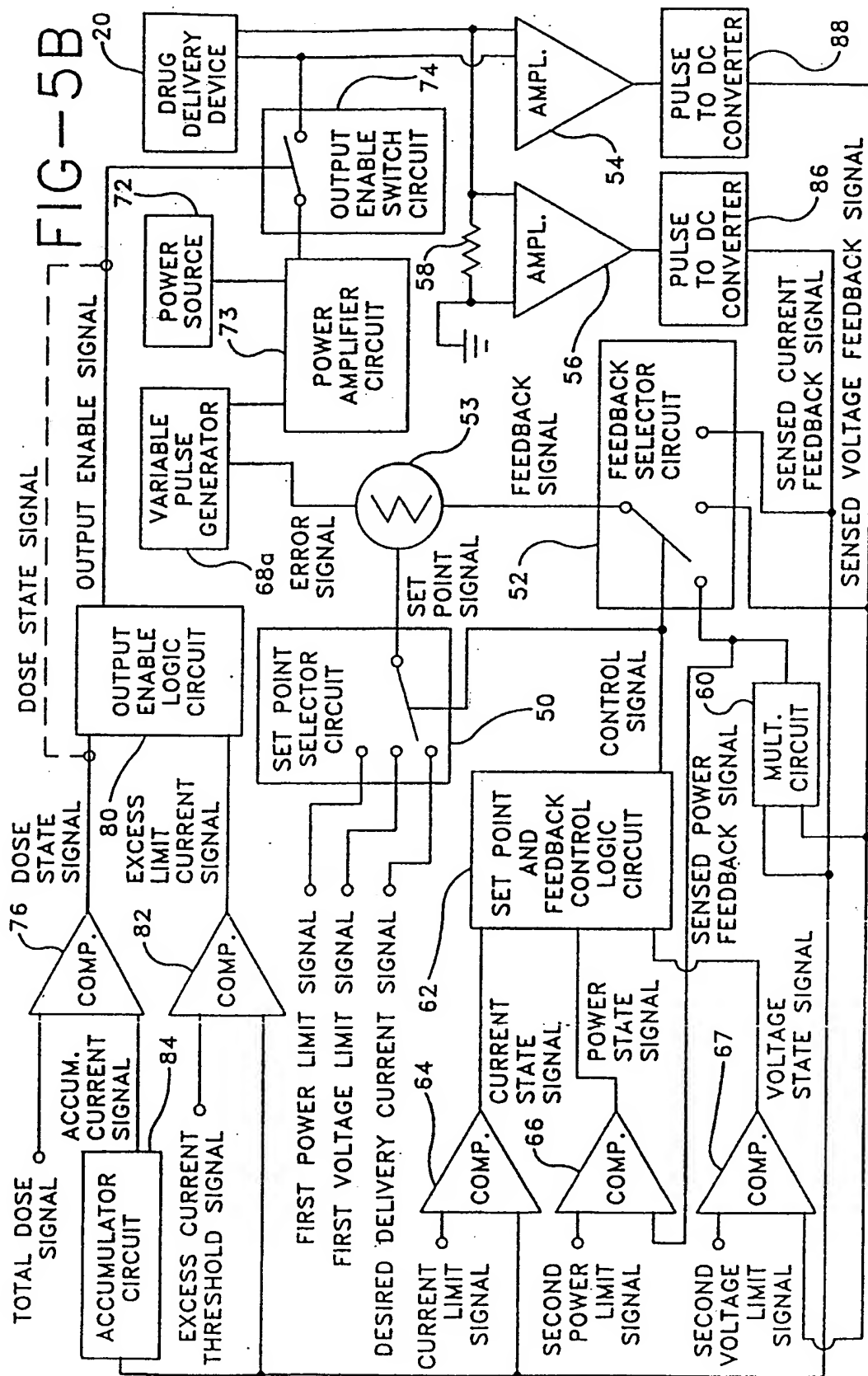


FIG-6

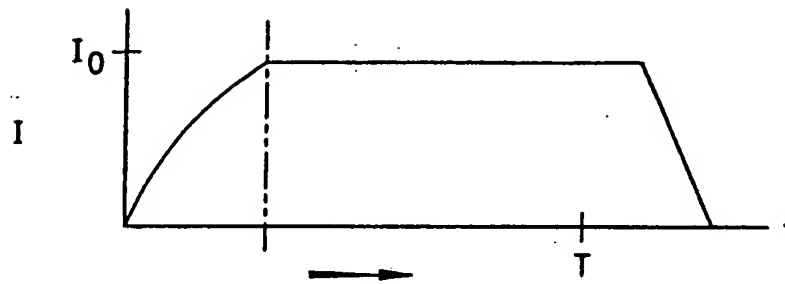


FIG-7

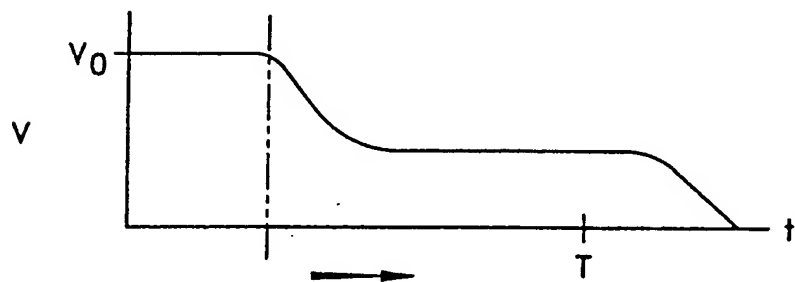
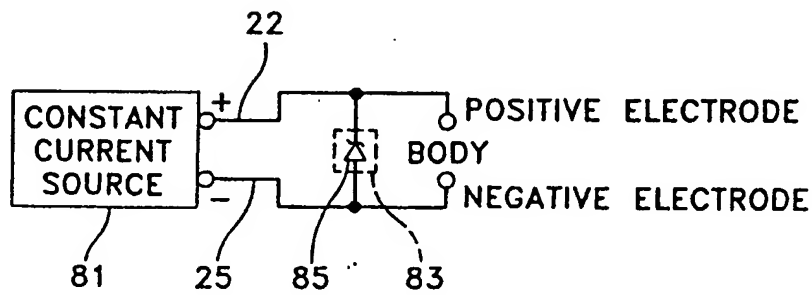


FIG-8



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